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CORRESPONDENCE

Response to letter re: Benefit from maintenance with PARP inhibitor in newly diagnosed ovarian cancer according to *BRCA1/2* mutation type and site: a multicenter real-world study
Not all *BRCA* mutations are equal: functional context and mutation type as co-determinants of PARP inhibitor response

We would like to express our gratitude to Prof. Arif Hakan Önder and Dr Mehmet Mutlu Çatlı for their interest and appreciation of our analysis. As they noted, our study found that in the *BRCA1*-mutated group, patients with mutations in the RING and BRCT functional domains (FDs) experienced more significant benefits from poly (ADP-ribose) polymerase inhibitors (PARPis). In contrast, among *BRCA2*-mutated patients, mutations in the RAD51-binding (BD) FD were associated with a higher response to olaparib.[1] It is important to emphasize that our findings only partially align with those from other similar studies.[2-4] Interestingly, although our population, like that of the PAOLA-1 subanalysis,[2] is predominantly Caucasian, we report a lower percentage of patients with the *BRCA1* mutation in the DNA-BD,[1] suggesting that further research is necessary before drawing definitive conclusions.

Nevertheless, we believe that the most relevant finding of our research is that patients with missense mutations, particularly those with the p.(Ala1708Glu) mutation, showed the most significant advantages from maintenance therapy with PARPi and did not experience a recurrence. This indicates the potential for interindividual variability in PARPi response among *BRCA* mutation carriers, which could be explained by the combination of the location and type of *BRCA* mutations. It supports the idea that the same kind of mutation may have different effects depending on its specific site, and vice versa.[1-4]

Therefore, we strongly agree with Prof. Arif Hakan Önder and Dr Mehmet Mutlu Çatlı regarding the importance of integrating information about both the mutation domain and type. These data should be made available for each patient in future clinical trials, as well as real-world studies. It should be deeply investigated to be used eventually to tailor treatment approaches more effectively.

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Available online 29 May 2025

https://doi.org/10.1016/j.esmoop.2025.105299
DOI of original articles: https://doi.org/10.1016/j.esmoop.2025.105298
https://doi.org/10.1016/j.esmoop.2025.104533

FUNDING

None declared.

DISCLOSURE

CM has received grants or contracts from GSK, Pharmamar, Merck Sharpe & Dohme (MSD), Menarini, and AstraZeneca; has received consulting fees from GSK, Pharmamar, Clovis, MSD, AstraZeneca, and Arquer Diagnostics; has received support for attending meetings and/or travel from AstraZeneca and Roche; and has participated on a data safety monitoring board or advisory board for GSK, Pharmamar, Clovis, MSD, and AstraZeneca. AF has received grants or contracts from AstraZeneca and MSD; has received consulting fees from GSK, Pharmamar, Johnson & Johnson, and Fondazione Internazionale Menarini; and has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from Pharmamar and GSK. CC has received consulting fees and payment or honoraria for lectures from and has participated on a data safety monitoring board or advisory board for

AstraZeneca, GSK, Pharmamar, and MSD. LI has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from Ipsen and BMS. MTP has received support for attending meetings and/or travel from MSD and AstraZeneca. CMS has received consulting fees from GSK and AstraZeneca and has received support for attending meetings and/or travel from Pharmamar. EG has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from GSK and AstraZeneca, and has received support for attending meetings and/or travel from MSD. LV has received consulting fees from GSK and Pharmamar. SMB has received consulting fees from GSK, Pharmamar, and AstraZeneca, and has received support for attending meetings and/or travel from Pharmamar. VS has received consulting fees from MSD, GSK, Immunogen, and Menarini Stemlines, and has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from GSK, AstraZeneca, and MSD. MGF has received consulting fees from MSD Italia S.r.l., GSK, and AstraZeneca. CN has received consulting fees from Illumina and Guardant Health, MSD, GSK, AstraZeneca, Altems, and Veeva, and has received support for attending meetings and/or travel from MSD, Illumina, Menarini, and AstraZeneca. LM has received consulting fees from MSD and AstraZeneca. AR has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from Roche Diagnostics and has participated on a data safety monitoring board or advisory board for Bristol Myers Squibb, Pfizer, Bayer, and Kyowa Kirin. GS has received grants or contracts from Novartis, Lyra, Sofar, Galileo Research, Olympus, Merck KGAA, AstraZeneca, Celgene Corporation, Roche, Pharma Mar, Shionogi, Morphotek, Linnea, Cryolife, Celldex, Pfizer, Millenium, GSK, Llc, Princess Margaret Cancer Centre, Central And Eastern European Gynecologic Oncology Group (CEEGOG), K-Group Beta, Inc., S&R Pharmaceutic, MSD, Karyopharm Therapeutics, Novocure Ltd, Seattle Genetics Inc., Clovis Oncology, Inc, Immunogen, Inc, Bayer Ag, Inovio Pharmaceuticals Inc, Aeterna Zentaris Gmbh, Glycotope Gmbh, Eli Lilly, Sanofi-Aventis Recherche Et Développement, Tesaro, Inc., Novocure Ltd, Oncoquest Pharmaceuticals Inc, Kiromic, Medtronic, Advenchen Laboratories, Merck, Debiopharm, Arcagy Gineco, Consorzio Oncotech, Oncoquest Inc., and Transenterix Italia S.R.L.; has received consulting fees from Menarini, Olympus Europa, Intuitive Surgical, GSK, Covidien AG (Med Company), Baxter Healthcare, AstraZeneca, and MSD; and has received support for attending meetings and/or travel from Olympus Europa, Intuitive Surgical Inc, GSK, Covidien A (Medtronic company), Baxter Healthcare, AstraZeneca, and MSD. DL has received grants or contracts from Pharmaand, GSK, and MSD; has received consulting fees from GSK, MSD, AstraZeneca, Immunogen, Regeneron, Sutro, Genmab; and has received payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing, or educational events from GSK and MSD. All other authors have declared no conflicts of interest.

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